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10/541,019	06/28/2005	Akira Tsuji	Q88424	4031

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SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER	
PALENIK, JEFFREY T	
ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,019	TSUJI ET AL.	
	Examiner	Art Unit	
	Jeffrey T. Palenik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,14,17 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,14,17 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of Applicants' Amendments and Remarks filed 5 August 2008. The Examiner acknowledges the following:

Claims 10-13, 18 and 19 are cancelled. Further, in correction to that which was stated by the Examiner, in the previous Office Correspondence, claims 15, 16, 20 and 21 stand cancelled, not withdrawn from consideration. The Examiner thanks Applicants for clarifying the status of these claims.

Claims 1, 5 and 17 have been amended. New claim 22 has been added.

Where support for the amendments was not expressly provided, it was found either within Applicants' disclosure and/or originally filed claims (i.e. cancelled claim 12). The Examiner acknowledges that no new matter has been added to the claims.

Thus, claims 1-9, 14, 17 and 22 now represent all claims currently under consideration.

INFORMATION DISCLOSURE STATEMENT

No new Information Disclosure Statement (IDS) have been submitted for consideration.

WITHDRAWN OBJECTIONS/REJECTIONS

Objection to the Specification

Applicants' amendment to the Abstract of the Invention renders moot the objection. Thus, said objection has been **withdrawn**.

Objection to the Specification

Applicants' editorial amendment correcting the spelling of the term "glycine" renders moot the objection made to claim 9. Thus, said objection has been **withdrawn**.

Applicants' cancellation of claims 10 and 11 renders moot the objections made to claims 10 and 11. Thus, said objections have been **withdrawn**.

Rejections under 35 USC 112

Applicants' remarks regarding the terms "compound recognized by proton coupled transporters", "proton-coupled transporter" and "pH-sensitive polymer", render moot the written description rejections to claims 1-9, 14 and 17, under 35 USC 112, first paragraph. Thus, said rejections have been **withdrawn**.

Applicants' amendments and remarks regarding the recitations "a compound recognized by proton-coupled transporters and a pH-sensitive polymer" and "excellent", "optimum", and "β-alanine" render moot the rejections to claims 1, 9 and 17, under 35 USC 112, second paragraph. Thus, said rejections have been **withdrawn**.

Rejection under 35 USC 102(b)

Applicants' amendments to the instant claims, namely claims 1 and 17, render moot the rejection to claims 1-3, 8, 9, 14 and 17, under 35 USC 102(b) as being anticipated by Gaunt (USPN 3,148,124). Thus, said rejection has been **withdrawn**.

MAINTAINED REJECTIONS/OBJECTIONS

The following rejections are maintained from the previous Office Action dated 31 March 2008:

CLAIM REJECTIONS - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 12-14 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Behl et al. (U.S. Patent 4,525,339).

The instant claims 1 and 17 are drawn to a gastrointestinally-absorbed, pharmaceutical preparation comprising 1) a compound recognized by a proton-coupled transporter and 2) a pH-sensitive polymer. Dependent claims 2-4 are directed to a peptide-specific proton-coupled transporter. Dependent claim 5 further limits claim 4 by reciting compounds recognized by the peptide transporter. Dependent claim 6 recites limitations to the composition of claim 3 such that the proton-coupled transporter is a monocarboxylic acid transporter. Dependent claim 7 further limits claim 6 by reciting compounds recognized by the monocarboxylic acid transporter. Claims 12 and 13 both recite limitations to the pH-sensitive polymer of the composition. Claim 14 recites the composition of claim 1, further limiting it to an oral dosage form.

Behl et al. teaches an orally administered enteric coated pharmaceutical composition which consists essentially of a beta-lactam antibiotic admixed with an enhancer consisting of a C_2 to C_{12} glyceride mixture with fatty acids having a length of C_2 to C_{12} (claim 1). Examples of C_2 to C_{12} fatty acids admixed with glycerides that are taught include butyric acid (col. 10, lines 20-30). Table 3 also teaches the use of monoglyceride of acetic acid (e.g. Enteral monoacetin). Enteric coatings that are taught include methacrylic acid copolymers L and S (e.g. Eudragit L and S) (col. 10, lines 58-65; col. 11, lines 1-30).

RESPONSE TO ARGUMENTS

Applicants' arguments with regard to the rejection of claims 1-7, 14 and 17 under 35 USC 102(b) as being anticipated by Behl, has been fully considered, but is not persuasive.

Applicants allege that Behl does not teach or suggest the specific combination of β-lactam antibiotics and a pH-sensitive polymer.

In response, the Examiner respectfully submits that Behl expressly teaches the combination of β-lactam antibiotics and a pH-sensitive polymer. Claims 1, 9 and 10 are directed to an orally administered enteric coated pharmaceutical compositions comprising a β-lactam antibiotic distributed throughout. Several specific examples of enteric coatings are taught in the Table presented by Behl at col. 11, lines 1-30, the last example of which comprises Eudragit S or L (i.e. methacrylic copolymers S or L) at 8% (w/w). The teachings of Behl et al. are still considered by the Examiner as reading on the rejected claims.

Thus, for these reasons, Applicants' arguments are found unpersuasive. The above rejection is hereby **maintained**.

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-9, 12-14 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Behl et al. (U.S. Patent 4,525,339) in view of Gaunt (U.S. Patent 3,148,124).

The instant claims are drawn to an orally-administered, gastrointestinally-aborbed, pharmaceutical preparation, as described above.

Such compositions are taught by Behl et al., as earlier described.

Behl et al., however, does not teach the limitation of the instant claims wherein compounds are recognized by amino acid transporters transporting D-cycloserine such as alanine, L-proline, or glycine.

The invention of Gaunt teaches the preparation of oral dosage formulations comprising water-soluble medicaments further comprising at least one non-reactive water-

soluble carrier such as glycine and pH-sensitive materials (e.g. polyacrylic acid), also as described above.

In view of the combined teachings of the prior art, one of ordinary skill in the pharmaceutical art would have been motivated to prepare an enteric-coated drug formulation whose composition contained both a compound recognized by a proton-coupled transporter and a pH-sensitive polymer with a reasonable expectation of controlling the release of the admixed medicament. Such would have been obvious in the absence of evidence to the contrary because Behl et al. teaches glycol compounds as alternative enhancers to compounds such as butyric acid (col. 2, lines 16-29). Gaunt teaches water-soluble glycol as an alternative carrier to glycine, in claim 6. Therefore, modification of the invention of Behl et al. to substitute glycine for a glycol compound as a release enhancer is well within the purview of the skilled artisan. Furthermore, a person of ordinary skill in the art would have been motivated, with minimal undue experimentation, to make the necessary result-effective modifications thus enabling the required delay of drug release from the composition by adjusting parameters such as the compound recognized by the transporters in the small-intestinal epithelial cells, and reasonably would have expected success because the prior art teaches the mixing of different combinations of pH-sensitive polymers and compounds recognized by cellular transporters.

RESPONSE TO ARGUMENTS

Applicants' arguments with regard to the rejection of clams 1-9, 14 and 17 under 103 over Behl in view of Gaunt et al. have been fully considered but they are not persuasive.

Applicant alleges that the composition of claim 1 not only recites a new composition (i.e. is novel and unobvious over the cited references), but also provides notable effects (i.e. effects (i) to (iv) on page 17 of the response) as well as Examples cited with the instant disclosure (i.e. Examples 3 and 4) which discuss properties of the instantly claimed composition. Applicants attest that neither of the aforementioned are recognized by the cited references.

In response to Applicants' argument that the references fail to show certain features of Applicants' invention, it is noted that the features upon which Applicants rely (i.e., "notable effects" (i) through (iv) and the "unexpected results" evidenced by Examples 3 and 4 of the specification) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Additionally, the evidence provided by Applicants in Example 3 discusses limited properties of the composition, notably using Eudragit L100-55. Example 4, discusses using Eudragit L100-55 or Eudragit RS PO, the latter of which is not within the scope of the instant claims. The instant claims 1 and 17 recite alternative limitations to the former which continue to be read upon by the combination of the cited references.

In response to Applicants' argument that the composition recited in the instantly amended claim 1 "provides … notable effects", the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Thus, in response, the Examiner respectfully submits that the cited references continue to teach and render obvious the instantly claimed compositions and that the "notable effects" are functional properties and that until some material differences in the properties of the composition are demonstrated, the alleged functional limitations are considered by the Examiner to be directed toward the composition which is instantly claimed.

For these reasons, Applicants' arguments are found unpersuasive. Said rejection is therefore **maintained**.

NEW REJECTIONS

In light of Applicants' amendments, most notably to claims 1 and 17, as well as the addition of new claim 22, the following rejections have been newly added:

CLAIM REJECTIONS - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-9, 12-14, 17 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Behl et al. (U.S. Patent 4,525,339) in view of Gaunt (U.S. Patent 3,148,124).

The instant claims are drawn to an orally-administered, gastrointestinally-aborbed, pharmaceutical preparation, as described above. New claim 22 is directed to a limitation which further narrows the range of pH-sensitive polymer to 10-20% base on the weight of the entire preparation.

The teachings to both Behl et al. and Gaunt are discussed above.

Neither of the references expressly teach the narrower range of the pH-sensitive polymer, as claimed by Applicants. Since the values and formats of each parameter with respect to the claimed composition are adjustable, it follows that each is a result-effective parameter that a person having ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. For example, the reference to Behl teaches that the amount of coating per preparation is adjustable (col. 11, lines 31-33). Thus, it would have been customary for an artisan of ordinary skill, to adjust the amount of pH-sensitive polymer within the composition, in order to achieve the desired claimed final composition. Thus, absent some demonstration of unexpected results from the claimed parameters, optimization of any of these parameters would have been obvious at the time of Applicants' invention.

All claims have been rejected; no claims are allowed.

CONCLUSION

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey T. Palenik whose telephone number is (571) 270-1966. The examiner can normally be reached on 7:30 am - 5:00 pm; M-F (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published

applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Palenik/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615